Appendixes

Appendix A
Federal Spending for Mutation Research

A quick review of the origins of biotechnology illustrates the difficulty of identifying the specificareas of research that would further our knowledge of human mutations, and, in turn, the problems of estimating the current amount of Federal expenditures for such research.

In *1968* and 1969, Hamilton O. Smith, a microbiologist at Johns Hopkins University, had no thought of studying human heritable mutations. No venture capital firm was looking for biotechnology companies to invest in, and had it been, it would have been disappointed. No such company existed,

Smith was studying how some bacteria can take up molecules of DNA from their growth medium and recombine it into their genetic material. He knew that the bacteria would not take up DNA from other species of bacteria or from viruses, and he added some viral DNA to the experiment expecting that it would remain inert and intact while the bacterial DNA underwent recombination. Instead, the viral DNA was rapidly degraded. Looking at that result, Smith hypothesized that a bacterial enzyme(s) could discriminate between foreign DNA (from the virus), which it degraded and self DNA (from the same kind of bacteria), which it left alone. He purified the enzyme and showed that it recognized particular sequences of nucleotides on the viral DNA and cut it at those sites (128).

These experiments, which identified and characterized the first known restriction enzyme, opened the door to the discovery of hundreds of others. The use of restriction enzymes, allowing precise cutting of DNA and precise joining of DNA pieces from different parts of an organism's genome as well as joining of pieces from different organisms, led to fundamental advances in the basic approach of research in molecular biology and genetics (146,147). Accordingly, these enzymes are basic ingredients of the new technologies for studying human heritable mutations described in this report,

However, someone in **1969** who had tried to identify research projects that would contribute to our understanding of human mutation rates would almost certainly not have included Smith's. His was basic research directed at understanding the mechanism of recombination in an organism far removed from humans. This OTA report provides additional examples of the difficulty of estimating how much money is being spent on research that may be important to understanding human mutations.

Current Federal Expenditures for Mutation Research

OTA queried Federal research and regulatory agencies about their support of research directed at understanding human mutations. Questions were asked about the amount of money spent specifically on human mutation research and the amount spent on "related" areas of biological research. The first category was tightly defined—the research had to focus on development or applications of methods for detecting and/or counting human somatic or heritable mutations in vivo. The category of "related" research was much broader, including studies examining genetic contributions to such common diseases as diabetes and arthritis, studies of mutagenesis and repair mechanisms, development of instruments for measuring cellular effects of various kinds, and tests for mutagenic activity in lower organisms as well as in cultured human cells.

The expenditures shown in table A-1 must be treated with some reservation about their accuracy, the total of $14.3 million estimated as the amount spent on human mutation research being more precise than the approximately *$207* million estimated for related genetic research. The $14.3 million may be an overestimate—

Table A-1 .—Federal Expenditures for Research Related to Human Mutations

Federal aqency	Human mutation research	Related genetic research
Department of Energy	$ 6,220,000[a]	$ 30,123,000
Department of Health and Human Services:		
Centers for Disease Control	277,000	1,387.000
National Institutes of Health,	7,244,000[b]	156,959,000[c]
Food and Drug Administration		1,200,000
Environmental Protection Agency	606,000	1,189,000
National Science Foundation	0	16,336,000
Total	14,347,000	207,194,000

[a]This includes $1 .850000(or half of the total $3 700,000 at current exchange rates) spent annually for the U S contribution to the Radiation Effects Research Foundation the group that coordinates ongoing genetic studies of the survivors of the Nagasaki and Hiroshima bombings and their offspring

[b]This total was obtained by inspecting grant titles and reading grant abstracts *to identify those* that focused on human mutation research

[c]This figure is the budget for the Genetics Program in the National Institute Of General Medical Sciences It does not include all genetics research at NIH some of which goes on m other Institutes

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some projects studying clinical effects of mutations may provide no information about detection—and the $207 million for related genetic research is probably an underestimate, since much genetic research is supported by parts of the National Institutes of Health (NIH) not queried. For comparison, the total NIH budget for the fiscal year 1985 was about $4 billion. Most of the NIH funding for mutation research is directed at identifying mutations in at-risk families (where specific tests for specific mutations are appropriate), whereas DOE supports **a** search for more general methods to detect mutations.

Successes of the research efforts in human mutation research and related genetic research will probably generate a requirement for additional funding in the near future. It will be a costly venture to take any new technique (such as those described inch. 4) and apply it to studies of populations sufficiently large to provide a good possibility of yielding information about human mutations. For instance, the ongoing monitoring of the Nagasaki and Hiroshima populations using clinical examinations and protein analyses (see ch. 3) costs about *$3.7* million annually to the U.S. and Japanese governments together (48).